

/KRS/ 10/27/2009

Amended Claim Set

1. (Cancelled)
2. (Previously Presented) The method according to claim 34, wherein the motif or the combination of motifs is a nucleotide or a combination of nucleotides and a subset of sequences is selected from sequences in a databank of nucleic acids.
3. (Previously Presented) The method according to claim 34, wherein the motif or the combination of motifs is an amino acid or a combination of amino acids and a subset of sequences is selected from sequences in a databank of polypeptides or proteins.
4. (Previously Presented) The method according to claim 34, wherein the reference sequence is a wild-type sequence.
5. (Previously Presented) The method according to claim 34, wherein the reference sequence is a sequence comprising in a position i a motif present in position i in a predetermined number of sequences of step (a).
6. (Cancelled)
7. (Previously Presented) The method according to claim 34, wherein positions of at least one of the sets E and F are designated by the user.
8. (Previously Presented) The method according to claim 34, wherein step (b) further comprises a test step including generating a totality of combinations of possible positions, determining for each of said combinations the value of coefficients R_R or R_F , and retaining the combination corresponding to a largest set of positions coefficient R_E or R_F of which corresponds to said second value.

9. (Previously Presented) The method according to claim 34, wherein the set of sequences comprises sequences of motifs of pathogenic organisms having a high level of mutability.

10. (Previously Presented) The method according to claim 34, wherein the set of sequences comprises sequences of motifs of genes implicated in human, animal or plant pathologies having a high level of mutability.

11.-19. (Cancelled)

20. (Currently Amended) The method according to claim 34, wherein the set of sequences of step (a) comprises all polypeptide sequences of different variants of a protease of human immunodeficiency virus.

21.-27. (Cancelled)

28. (Previously Presented) The method according to claim 34, further comprising, after step (c), a step (e) of comparing motifs identified in step (c) with known drug resistances to observed mutations.

29. (Previously Presented) The method according to claim 34, further comprising, after step (c), a step (e) of comparing motifs identified in step (c) with motifs of sequences implicated in at least one of a catalytic site and a site linked by noncompetitive inhibitors.

30.-32. (Cancelled)

33. (Previously Presented) The method of Claim 35, wherein the CLUSTAL algorithm is the CLUSTAL W algorithm.

34. (Previously Presented) A method for identifying a motif or a combination of motifs having a Boolean state of predetermined mutations in a set of sequences comprising:

a) aligning a set of sequences of ordered motifs represented by a single-character code on a programmed computer using a multiple sequence alignment program,

b) comparing a reference sequence with the set of sequences aligned in step (a) by forming a first numerical matrix A of dimensions $N \times M$ in which N designates a number of sequences and M designates a number of motifs of one sequence of said alignment, with value $A_{i,j}$ being equal to a first value $A1$ when the motif of position i of sequence j with a value ranging from 0 to N is mutated in relation to a motif of position i of the reference sequence and equal to a second value $A2$ in other cases,

forming two analysis matrices B and C of mutations in which:

— matrix B is a matrix of unmutated couples, of couples which do not mutate simultaneously, of dimension $M \times M$, value $B_{i,k} = B_{k,i}$ being equal:

- to a first value $B1$ when $A_{i,j} = A_{k,j} = A1$ irrespective of the value of j ranging from 0 to N ,
- to a second value $B2$ in other cases;

— matrix C is a matrix of mutated couples of dimension $M \times M$, value $C_{k,i} = C_{i,k}$ being equal:

- to a second value $C1$ when $A_{i,j} = A_{k,j}$ irrespective of the value of j ranging from 0 to N ,
- to a first value $C2$ in other cases;

determining for a set E of positions a coefficient R_E whose value is R_1 when values $B_{i,k}$ are equal to a second value $B2$, irrespective of the values of i and k belonging to set E of said positions,

determining for a set F of positions, a coefficient R_F , the value of which is R_1 when values $C_{i,k}$ are equal to second value $C2$, irrespective of the values of i and k belonging to set F of said positions;

wherein in the matrices, i and k designate positions and j designates a sequence, and

c) identifying motifs not having mutated simultaneously or motifs having mutated simultaneously at least once on at least one sequence of the set and not having mutated on another sequence of said set.

35. (Previously Presented) A method for identifying a motif or a combination of motifs having a Boolean state of predetermined mutations in a set of sequences comprising:

a) aligning a set of sequences of ordered motifs represented by a single-character code on a programmed computer using a CLUSTAL algorithm based multiple sequence alignment program or a Hidden Markov Model algorithm based multiple sequence alignment program,

b) comparing a reference sequence with the set of sequences aligned in step (a) by forming a first numerical matrix A of dimensions NxM in which N designates a number of sequences and M designates a number of motifs of one sequence of said alignment, with value A_{ij} being equal to a first value A1 when the motif of position i of sequence j with a value ranging from 0 to N is mutated in relation to a motif of position i of the reference sequence and equal to a second value A2 in other cases,

forming two analysis matrices B and C of mutations in which:

— matrix B is a matrix of unmutated couples, of couples which do not mutate simultaneously, of dimension MxM, value $B_{i,k} = B_{k,i}$ being equal:

- to a first value B1 when $A_{i,j} = A_{k,j} = A1$ irrespective of the value of j ranging from 0 to N,
- to a second value B2 in other cases;

— matrix C is a matrix of mutated couples of dimension MxM, value $C_{k,j} = C_{i,k}$ being equal:

- to a second value C1 when $A_{i,j} = A_{k,j}$ irrespective of the value of j ranging from 0 to N,
- to a first value C2 in other cases;

determining for a set E of positions a coefficient R_E whose value is R_1 when values $B_{i,k}$ are equal to a second value B2, irrespective of the values of i and k belonging to set E of said positions,

determining for a set F of positions, a coefficient R_F , the value of which is R_1 when values $C_{i,k}$ are equal to second value C2, irrespective of the values of i and k belonging to set F of said positions;

wherein in the matrices, i and k designate positions and j designates a sequence, and

c) identifying motifs not having mutated simultaneously or motifs having mutated simultaneously at least once on at least one sequence of the set and not having mutated on another sequence of said set.